REMARKS

Claims 1-120 have been canceled. Claims 121-158 are pending and are currently under consideration.

A. Interview Summary

Applicants thank Examiner Rawlings and Supervisory Examiner Helms for the telephone interviews of September 20, 2006, continuing to September 21, 2006, in which the claims, the content of the specification and the rejections of record were discussed as follows:

1. Figures 8 and 9, which illustrate binding of modified antibodies to denatured collagen over native collagen. Applicants also pointed the Examiner to paragraph [0036] of the application which discloses antibodies having a higher binding affinity for denatured collagen versus native collagen. In view of the disclosure of the specification and the data presented in Figures 8 and 9, Examiner Rawlings and Supervisory Patent Examiner Helms acknowledged that the application provides working examples of modified antibodies having higher binding affinity for denatured collagen versus native collagen and agreed that the claims do not have to recite "at least 2-fold" higher binding affinity.

Independent claims 121 and 131 recite an antibody, or antigen-binding fragment thereof, which has higher binding activity for denatured collagen over native collagen. New claim 141 recites the elected species of an antibody, or antigen-binding fragment thereof, which binds to denatured collagen as described in the specification. The antibodies or antigen-binding fragments thereof, recited in the current claims have a function associated with the structure.

2. During the interview, Applicants discussed Figures 4C and 6 of the application with Examiner Rawlings and Supervisory Patent Examiner Helms. Modifications of amino acid residues in one or more heavy and/or light chain CDRs of HUIV26 variants presented in the figures represent modifications made as compared to the wild-type sequence. Furthermore, Applicants faxed the Examiner a series of Tables which illustrated modifications made to heavy and light chain CDRs and which included references to the sequence identifiers containing the modifications. Applicants provide these Tables with this response as Exhibit A for entry into the file. The application demonstrates, therefore, possession of a genus of antibodies which are supported by sequences of

modified CDRs presented in the Figures, the description and the Sequence Listing. Applicants have shown how to make and use modified antibodies over the full scope of the claims using the methods described in the application. For these reasons, Applicants asserts that the claims are enabled over the full scope of the claims, have written support throughout the application, and that no new matter has been added by amendment in contrast to the Examiner's assertions of record.

In the interview, the Examiner indicated that the modifications (discussed above) presented in the Examiner's proposed amendment were found in Figure 4C of the application. As discussed in the interview, Applicants respectfully submit that the application contains more modifications in the CDRs than found in Figure 4C. Support for other CDR modifications can be found, for example, in Figure 6, in paragraphs [0043], [0049] and [0061] to [0078] of the published application, the originally-filed claims and the Sequence Listing as indicated in Exhibit A. Because the specification, as a whole, includes modifications which were not presented in the Examiner's proposed amendment, Applicants reserved the right to file a response to the Final Office Action rather than accept the Examiner's amendment.

3. Applicants thank Examiner Rawlings for acknowledging that the modified HUIV26 antibodies are novel and for agreeing to allow composition claims of antibodies reciting specific combinations of CDRs which were presented in the specification.

4. Applicants thank Examiner Rawlings and Supervisory Patent Examiner Helms for acknowledging that the application provides examples of modified antibodies having conservative and/or non-conservative modifications.

5. In response to the Examiner's previous statements of record, that the structure of variant of DhuG5 of Figure 8 was not presented in the specification, Applicants directed the Examiner to Figure 6 and discussed the Figure with respect to modifications made compared to the wild-type sequence CDRs. Applicants thank Examiner Rawlings and Supervisory Patent Examiner Helms for acknowledging that the structures of all of the variants presented have been disclosed, either in the specification, the Figures, and/or the Sequence Listing showing possession of the claimed compositions.

Thus, no new matter has been recited in the claims presented, or in the claims of record. Furthermore, Applicants have not made any additions to the specification.

6. Applicants submit that the claims have been amended solely to further prosecution; such amendments are not to be taken as acquiescence to the Examiner's rejections. Applicants reserve the right to prosecute any canceled subject matter in continuing and/or divisional applications.

B. Support for the new claims

The claims as currently recited are not broader than those previously filed of record. The newly submitted claims recite one or more specific modifications made in each of the CDRs, which modifications are explicitly recited in the application as filed.

Specific, non-limiting examples of support for the claims as recited are provided below:

- Specific support for all of the modifications made to the CDRs can be found, for example, in the claims, as originally filed, Figure 4C, Figure 6, the sequence listing, as originally filed, and in paragraphs [0049], [0052] and [0060] to [0078]. As discussed above, Applicants provide herewith the tables of modifications discussed during the interview in which Applicants pointed out support for modifications represented in the specification, the figures and the sequence listing (Exhibit A). Each of the amino acid modifications recited in the claims herein can be found in one or more of these locations. (Claims 121 and 131.)
- New claim 141 recites the elected species of record; support can be found in original claim 17.
- One finds the elected species of new claim 141 in independent claims 121 and 131 which recite a(n) (grafted) antibody, or antigen-binding fragment thereof, wherein *at least one* of the CDRs in the heavy chain variable region or the light chain variable region comprises a heavy chain CDR1 having a substitution of serine at position 10 by threonine (i.e., SEQ ID NO: 26 to SEQ ID NO: 45); a heavy chain CDR2 having a substitution of isoleucine at position 9 by alanine and of serine at position 14 by tyrosine (i.e., SEQ ID NO: 28 to SEQ ID NO: 155); a heavy chain CDR3 having a substitution of tyrosine at position 11 by proline (i.e., SEQ ID NO: 30 to SEQ ID NO: 63); a light chain CDR1 having a substitution of serine

at position 9 by tryptophan and of glycine at position 10 by tyrosine (i.e., SEQ ID NO: 20 to SEQ ID NO: 157); a light chain CDR2 of SEQ ID NO: 22 (i.e., no substitutions); and a light chain CDR3 having a substitution of serine at position 5 by glutamine (i.e., SEQ ID NO: 24 to SEQ ID NO: 77). That is, the (grafted) antibodies, or antigen-binding fragments thereof, of claim 121 and 131 have *one or more* substitutions and encompass the elected species.

- Support for the antibodies, or antigen-binding fragments thereof, of claims 142-158 can be found in paragraphs [0061] to [0078] of the application as filed.
- Support for the recited element of "higher" binding affinity for denatured collagen over native collagen was discussed during the interview, and can be found at, for example, in paragraph [0036] and in Figure 8 of the application. (Claims 121 and 131.)
- Support for grafted antibodies can be found, for example, at paragraphs [0095] to [0097] and in Example V of the specification. (Claims 122, and 131 to 140.)
- Support for antigen-binding fragments of antibodies, can be found, for example, at paragraphs [0029] and [0030] of the specification. (Claims 121-141.)
- Support for an antibody, or antigen-binding fragment thereof, having two CDR modifications can be found at, for example, paragraphs [0046], [0050], [0059], and [0061] of the specification. (Claims 124 and 137.)
- Support for an antibody, or antigen-binding fragment thereof, having three CDR modifications can be found at, for example, paragraphs [0062], [0063] and [0078] of the specification. (Claims 125 and 138.)
- Support for an antibody, or antigen-binding fragment thereof, having four CDR modifications can be found at, for example, paragraphs [0065], [0067], [0069] and [0074] of the specification. (Claims 126 and 139.)
- Support for an antibody, or antigen-binding fragment thereof, having five CDR modifications can be found at, for example, paragraphs [0064], [0066], [0068], [0071] to [0073] and [0075] to [0077] of the specification. (Claims 127 and 140.)
- Support for nucleic acids can be found, for example, at paragraphs [0028] and [0153] to [0155] of the specification. (Claims 128 and 134.)

- Support for antibodies further comprising therapeutic or detectable moieties can be found, for example, at paragraph [0170] of the specification. (Claims 129, 130, 135 and 136)

As all of the amendments are supported by the original disclosure, no new matter has been added. The above amendments have been made for reasons unrelated to patentability and should not be construed as constituting any admission with respect to the patentability of the previously claimed subject matter. By way of amendment, Applicants have cancelled claims 1-120 without prejudice or disclaimer to the subject matter therein. Upon entry of the foregoing amendments, new claims 121-141 are currently pending. Applicants assert that this Amendment has rendered moot the Examiner's rejections to claims 1-120 outlined above.

C. 35 U.S.C. § 112, 1, scope of enablement

1. As discussed during the interviews, the specification contains a dense amount of information describing how to make and use antibodies having modified sequences. Briefly, the specification fully recites how to make and use the antibodies as currently recited: see, for example, paragraphs [0098] to [0180], Examples III, IV, and VI and Figures 6-11.

With respect to the structure of the recited antibodies, the specification recites a representative number of species of antibodies, or antigen-binding fragments thereof, having CDRs containing conservative modifications, non-conservative modifications, or a combination thereof, that were made using the techniques described in the Detailed Description and Examples.

With respect to the function of the recited antibodies, Figure 6 illustrates that the modified antibodies, and antigen-binding fragments thereof, are able to bind denatured collagen as demonstrated by the association and dissociation rates. Figure 8 illustrates that modified antibodies, and antigen-binding fragments thereof, made using the methods recited in the specification bind with higher affinity to denatured collagen over native collagen.

2. Solely in an effort to further prosecution, Applicants have amended the claims to recite antibodies having at least one modification in at least one CDR wherein the specific substitutions are provided in the application and to remove the recitation of "at least 2-fold" higher binding affinity in view of the discussions above. However, Applicants maintain for the reasons of record that the claims as previously filed are fully enabled.

Based on the disclosure of the specification, including the Examples, Tables, Figures and Sequence Listing, Applicants submit that Examiner Rawlings and Supervisory Examiner Helms agreed during the telephonic interviews of September 20 and 21, 2006, that the claims as recited are fully supported. That is, the specification fully describes how to make and use such antibodies as currently claimed.

Applicants submit that the rejection of the claims under 35 U.S.C. § 112, first paragraph, is moot based on these amendments, and respectfully request that the rejections of claims under 35 U.S.C. § 112, ¶ 1, scope of enablement be withdrawn.

D. 35 U.S.C. § 112, 1 – Written Description

Applicants' position regarding the application and express support for the claims as currently recited has been discussed above.

Solely in an effort to further prosecution, Applicants have amended the claims as discussed above. The application clearly demonstrates that Applicants invented and were in possession of what is claimed based on the written description guidelines. Applicants maintain for the reasons of record that the claims as previously filed are fully supported by the application.

Applicants submit that the rejection of the claims under 35 U.S.C. § 112, first paragraph, is moot based on these amendments, and respectfully request that the rejections of claims under 35 U.S.C. § 112, ¶ 1, written description be withdrawn.

E. 35 U.S.C. § 112, 1st paragraph, new matter

As discussed in the interviews of September 20 and 21, 2006, and above, the application provides express support for the recited antibodies having higher binding affinity to denatured collagen over native collagen. As shown above, express support for the antibodies recited in the claims can be found in section B. Applicants have not made additions to the specification.

Applicants respectfully submit that the rejection is, therefore, moot and respectfully request withdrawal of the rejection.

CONCLUSION

Applicants believe that for the reasons set forth above, the Examiner's rejection of the claims have been overcome. Thus, Applicants respectfully request that the Examiner allow the composition claims and rejoin the method claims.

The Commissioner is authorized to charge any additional fees which may be required, including petition fees and extension of time fees, to Deposit Account No. 23-2415 (referencing 30797-711.201).

The Examiner is invited to call the undersigned agent at 858.350.2300 with any questions.

Respectfully submitted,

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